Respiratory Physiology & Neurobiology 218 (2015) 46–56

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

CO_2 pulse and acid-base status during increasing work rate exercise in health and disease

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ARTICLE INFO

Article history:
Received 17 May 2015
Received in revised form 26 June 2015
Accepted 12 July 2015
Available online 28 July 2015

Keywords:
Hydrogen ion
Buffering
Anaerobic threshold
Lactic acidosis
Cardiopulmonary exercise testing

ABSTRACT

The CO_2 pulse ($\dot{V}CO_2$/heart rate), analogous to the O_2 pulse ($\dot{V}O_2$/heart rate), was calculated during cardiopulmonary exercise testing and evaluated in normal and diseased states. Our aim was to define its application in its release in excess of that from $\dot{V}CO_2$/heart rate in the presence of impaired cardiovascular and lung function. In the current study, forty-five patients were divided into six physiological states: normal, exercise-induced myocardial ischemia, chronic heart failure, pulmonary vasculopathy, chronic obstructive pulmonary disease, and interstitial lung disease. We subtracted the O_2 pulse from the CO_2 pulse to determine the exhaled CO_2 that could be attributed to CO_2 pulse of buffering of lactic acid. The difference between the CO_2 pulse and O_2 pulse ($\dot{V}CO_2$/heart rate–$\dot{V}O_2$/heart rate) includes CO_2 generated from HCO_3^- buffering of lactic acid. The accumulated CO_2 per body mass was found to be significantly correlated with the corresponding [HCO_3^-] decrease ($R^2 = 0.72$; $P < 0.0001$). In summary, the increase in CO_2 pulse over the O_2 pulse accounted for the anaerobically-generated excess-CO_2 in each of the physiological states and correlated with the decreases in the arterial Bicarbonate concentration.

1. Introduction

Quantitative gas exchange measurements have been of value for selecting patients for heart transplantation (Guazzi, 2002; Mancini et al., 1991; Stevenson et al., 2008). Additional measurements, such as the anaerobic threshold (*AT*), also referred to as lactic acidosis threshold (LAT), has been of clinical value for identifying patients at high risk of death for major surgery (Grocott and Pearse, 2010; Older et al., 1999). There are various additional clinical applications of the *AT* in different diseases (Rossiter, 2011; Thirapatarapong et al., 2014). During the past 30 years, there have been increased numbers of reports showing that cardiopulmonary exercise testing (CPET) provided valuable information on the severity of graded heart failure (Guazzi et al., 2015; Myers et al., 2008; Sun et al., 2010; Wasserman et al., 2007). Also, CPET has been valuable in grading severity of pulmonary vascular disease (Dumitrescu et al., 2010; Yasunobu et al., 2005). It is also accepted that CPET is a valuable tool to the non-invasive diagnostic workup of patients with symptoms of exercise intolerance (Georgiopoulou et al., 2012; Ramponi et al., 2013). The concept of the *AT* was developed approximately 50 years ago when addressing the exercise limitation in patients with heart failure (Wasserman and McIlroy, 1964). This concept was in agreement with findings from other groups (Hollmann, 1985). Gitt et al. (2002) showed that a reduced *AT*, with an increased ventilatory requirement for CO_2 elimination ($\dot{V}E/\dot{V}CO_2$), were strong predictors of early death (six months) in heart failure patients. Physiological assessments such as reduced O_2 pulse ($\dot{V}O_2$/HR) at peak exercise provide insight into the stroke volume response to exercise. There are critical opinions against the *AT* concept, stating that lactate does not increase as a threshold function, but increases as an exponential function. To repudiate this point of view, we analyzed the rate of lactate and pyruvate increase and the lactate-to-pyruvate ratio in previous studies. Lactate, pyruvate and its ratio increased more clearly as a threshold function than an exponential model (Wasserman et al., 1985; Wasserman and McIlroy, 1964). Further, we showed that the increase in lactate and lactate-to-pyruvate ratio preceded the increase in pyruvate.

The concentration of arterial bicarbonate ([HCO_3^-]) remains relatively constant as work rate increases up to the *AT*. Using a quantitative CPET is especially useful when the cause of exercise intolerance is due to reduced O_2 transport. In order to determine

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http://dx.doi.org/10.1016/j.resp.2015.07.005
1569-9048/

Table 1
Demographics and exercise gas exchange of study population.

Group	N	Age	Sex	Height	Weight	BMI	$\dot{V}O_2$ (L/min)			$\dot{V}CO_2$ (L/min)			RER			$\dot{V}CO_2/HR - \dot{V}O_2/HR$ (ml/beat)			$\dot{V}E/\dot{V}CO_2$			$P_{ET}O_2$ (mm Hg)			$P_{ET}CO_2$ (mm Hg)		
		(year)	(M/F)	(cm)	(kg)	(kg/m^2)	Rest	*AT*	Peak	Rest	*AT*	Peak	Rest	*AT*	Peak	Rest	*AT*	Peak	Rest	*AT*	Peak	Rest	*AT*	Peak	Rest	*AT*	Peak
Normal																											
Mean	9	46	7/2	168	71	25	0.30	1.17	2.30	0.27	1.03	2.98	0.91	0.87	1.29	−0.3	−1.3	3.7	37	27	32	108	98	118	36	44	37
SD		15		10	15	3	0.06	0.40	0.61	0.08	0.37	0.84	0.17	0.06	0.09	0.6	0.8	1.6	5	3	4	9	9	5	4	4	4
SEM		5		3	5	1	0.02	0.13	0.20	0.03	0.12	0.28	0.06	0.02	0.03	0.2	0.3	0.5	2	1	1	3	3	2	1	1	1
Exercise-induced myocardial ischemia																											
Mean	5	63[a]	5/0	176	79	26	0.30	1.14	1.71[a]	0.24	1.03	2.37	0.82	0.90	1.41	−0.7	−0.9	4.0	38	30	37	96	106	123	37	41	35
SD		6		5	12	5	0.09	0.17	0.42	0.08	0.21	0.43	0.12	0.05	0.21	0.5	0.4	1.1	9	3	6	35	12	7	3	3	6
SEM		3		2	5	2	0.04	0.08	0.19	0.03	0.09	0.19	0.06	0.02	0.10	0.2	0.2	0.5	4	1	3	16	5	3	1	2	3
Chronic heart failure																											
Mean	8	57	6/2	168	71	25	0.27	0.79[a]	1.22[b]	0.21	0.70[a]	1.43[b]	0.78[a]	0.88	1.16	−0.8	−0.9	1.5[b]	41	36[b]	40	108	109[a]	120	34	35[b]	32
SD		10		5	11	3	0.05	0.21	0.37	0.04	0.19	0.54	0.08	0.04	0.13	0.4	0.4	1.5	6	6	9	7	8	5	5	6	6
SEM		3		2	4	1	0.02	0.07	0.13	0.01	0.07	0.19	0.03	0.01	0.05	0.2	0.2	0.5	2	2	3	3	3	2	2	2	2
Pulmonary vasculopathy																											
Mean	6	57	5/1	172	72	24	0.29	0.84	1.36[b]	0.24	0.74	1.61[b]	0.84	0.87	1.20	−0.6	−1.0	1.7[b]	49[b]	43[b]	47[b]	113	112[b]	122	29[b]	32[b]	30
SD		6		9	13	3	0.02	0.28	0.45	0.04	0.28	0.50	0.14	0.06	0.16	0.6	0.4	1.2	8	5	15	11	6	9	6	5	10
SEM		2		4	5	1	0.01	0.12	0.19	0.02	0.11	0.20	0.06	0.03	0.07	0.2	0.2	0.5	3	2	6	4	2	4	2	2	4
Chronic obstructive pulmonary disease																											
Mean	9	51	9/0	175	84	27	0.30	0.83[a]	1.43[b]	0.26	0.75	1.72[b]	0.88	0.91	1.20	−0.4	−0.8	2.0[b]	44[a]	37[b]	41[a]	112	109[b]	119	33	36[b]	34
SD		11		4	14	5	0.09	0.20	0.47	0.08	0.15	0.59	0.10	0.09	0.09	0.4	0.9	1.1	6	8	11	8	10	13	5	7	11
SEM		4		1	5	2	0.03	0.07	0.16	0.03	0.05	0.20	0.03	0.03	0.03	0.1	0.3	0.4	2	3	4	3	3	4	2	2	4
Interstitial lung disease																											
Mean	8	41	5/3	170	67	23	0.27	0.95	1.40[b]	0.22	0.86	1.70[b]	0.79	0.92	1.27	−0.7	−0.8	1.9[b]	41	36[b]	41[a]	107	111[b]	123	35	36[a]	32
SD		16		12	17	3	0.07	0.51	0.65	0.07	0.42	0.65	0.12	0.07	0.20	0.6	0.9	1.0	6	5	6	7	6	4	4	5	3
SEM		6		4	6	1	0.02	0.18	0.23	0.02	0.15	0.23	0.04	0.02	0.07	0.2	0.3	0.4	2	2	2	2	2	1	1	2	1

BMI, body mass index; RER, respiratory exchange ratio equals $\dot{V}CO_2/\dot{V}O_2$.
[a] Difference from normal: $P < 0.05$.
[b] Difference from normal: $P < 0.01$.